REMARKS

The above-captioned patent application has been carefully reviewed in light of the final Office Action to which this Amendment is responsive. Claims 1 and 23 have been amended in an effort to more clearly define and particularly point out that which is regarded as the present invention. To that end, it is believed that no new matter has been added to the above-captioned application.

Claims 1-11, 23-27 and 31-34 are currently pending. Each of the pending claims have been rejected in light of certain prior art. More particularly, Claims 1-4, 7-11, 23-25 and 31-34 have been rejected under 35 USC §103(a) as being unpatentable over Killeen et al. (U.S. Patent No. 5,166,051) in view of Durst et al. (U.S. Patent No. 6,358,752 B1), and Claims 5-6 and 26-27 have been rejected based on the combination of Killeen et al., Durst et al. and further in view of Fruitstone et al. (U.S. Patent No. 4,259,207). Claims 1-11, 23-27 and 31-34 have also been rejected under 35 USC §112, 2nd paragraph. Applicant respectfully requests reconsideration on the amended claims and the following discussion.

In order to successfully maintain a "prima facie" obviousness rejection under the Statute, each and every claimed limitation must be found in or be suggested, either singly or in combination, by the cited prior art. Those features that are not found or are suggested by the prior art must be notoriously well known in the field of the invention at the time thereof. In addition, it is axiomatic that a motivation be fond in the prior art as a whole to one of sufficient skill in the field of the invention to make the purported combination. The motivation cannot be the result of impermissible hindsight; that is, advance knowledge of the invention wherein piecemeal substitution of features are made without regard to the entirety of the teachings of the cited art. Put another way, the purported combination cannot destroy or drastically change the teachings of the references, particularly when at least one reference teaches away from such a combination.

According to the present invention, a biosensor is described in which cell components in a liquid specimen are shrunk by contacting a cell shrinkage reagent. The cell components can permeate on a chromatography carrier of the biosensor with high efficiency and without permeation solution being added. This increases the amount of liquid that flows in the chromatography downstream direction. Therefore, and even in the case in which whole blood or bacteria solution are a liquid specimen that include cell components, a device is realized that can rapidly carry out a high precision analysis with a simple construction, with reduced costs and without preprocessing of the sample. In other words and according to the invention, the shrunk cell components (such as enthrocyte) move in the downstream direction on the chromatography carrier together with the liquid specimen or the analyte.

Turning to the cited prior art, and with regard to Killeen (U.S. Patent No. 5,166,051), which was also previously cited in the previous Office Action, it is believed the present invention is distinguishable.

First, the Examiner has stated that "Killeen et al. does not explicitly teach that the shrunk cell components are "chromatographically developed", the reference does not teach that crenated cells are immobilized immediately after being shrunk" (see page 4, lines 16-19 of this Office Action), and it appears that it is not clear whether the shrunk cell components move or not. However, we believe it is clear that cell components do not move according to the teachings of Killeen, for the following reasons:

First, Killeen teaches that since the presence of whole blood in the detection zone physically and chemically interferes with colorimetric assay procedures and also that since the red blood cells contain high-concentration hemoglobin, the free hemoglobin in the red blood cell or the melted blood also makes the measurement result at the detection region obscure. Further, Killeen also teaches that in an accurate and high precision dry test strip which is used rapidly, that the presence of red blood cells seriously impacts the qualitative and quantitative analysis in the detection region (see column 1, lines 31-50 of Killeen).

Second, Killeen describes a technique wherein exclusion membranes are provided that enable centrifugation, allowing solidification agents and the analytes to pass therethrough, but preventing the passage of red blood cells, in order that the red blood cells not be present in the detection zone. However, since the red blood cells cannot be removed completely, there are variations in the measurement and a resulting level of unreliability, wherein a system in which whole blood is used as a liquid specimen can be analyzed without being affected by red blood cells chemically and physically is desired (column 1, line 51 to column 2, line 13).

From the above teachings as described by Killeen, it must be understood that it is required that the red blood cells should not move to the detection region and it is further required that these cell components should preferably not move.

Further, as noted in the "SUMMARY" portion of Killeen, it is disclosed that the overlay membrane includes an effective amount of crenating agents in order to exclude the red blood cells, that the red blood cells become not flexible but solid by being crenated, and that these cells do not intrude into the detection region by the function of the pores of the detection region membrane (column 2, lines 23-26, lines 28-35).

Thus, we believe that the cell components do not move to the detection zone is fundamental to the teaching of Killeen.

In addition to the above, Killeen also teaches that this lack of movement of the red blood cells repletely in several portions of the disclosure. For example, the movement of the red blood cells is prevented by the pores of the detection zone membrane (see col. 4, lines 10-11); the membrane has no effect of blocking the red blood cells when pH is too high (col. 4, lines 46-47); and the overlay membrane is connected with the detection zone membrane, allowing the analytes to pass therethrough into the detection zone membrane, but not permitting the red blood cells to pass therethrough (column 5, lines 18-24).

From the preceding review of the cited reference, taken in its entirety, it is clear from Killeen that it is undesired and also similarly clear that the cell components do not move to the detection region.

Durst et al. discloses a test device in which detection or an assay is carried out for the analytes that are present in a test sample by utilizing the capture portion that is specifically combined with analytes.

The test device of Durst et al. employs two binding materials for the analytes, which are combined with different portions of the analytes. One of the above binding materials forms a capture portion that is fixed to the absorbent agent, while the other binding material is in a state of being combined with marker encapsulated liposomes, thereby enabling measurement on a sandwich reaction in the capture portion.

The Examiner has opined that this device is constituted by three absorbent agents consisting of a "first pad serving as both of the contact portion and the capture portion", a "second pad which absorbs liquid permeated from the first pad", and a "third pad having a capture portion". The Examiner further characterizes this reference wherein nitrocellulose is preferably employed for the absorbent agent having a capture portion (see Durst et al., col 7, line 60 to col 8, line 50). In addition, the test sample moves according to these devices by capillary action (see col. 10, lines 48-50), wherein only the analytes in the test sample that have permeated remain at the capture portion while the other substances permeate in the downstream direction. Still further and according to the Examiner, a mechanism by which analytes in the test sample are analyzed or assayed by the marker-liposomes at the capture portion being detected is taught (see col 6, DETAILED DESCRIPTION OF THE INVENTION).

The Examiner has still further characterized Durst et al. as teaching " a test strip with a capture portion 110 (i.e. reaction layer) downstream of layers 104 and 106, in order to provide immobilized probes that isolate analytes of interest allow other materials to flow past the capture portion" (see page 5, lines 8-10 of the Office Action), wherein the Examiner believes that the present invention can be realized by combining Durst et al. and Killeen.

However, many patent applications relating to a test strip have been filed prior to Durst et al. in which a reaction layer is located at a position toward downstream in the permeating direction relative to the position at which a test sample is applied, and the substances other than the analytes are permeated to a downstream region passing through the reaction layer. For example, EP 0284232 which was filed more than ten years prior to Durst et al., discloses a solid immunoassay that employs an insoluble granular marker, such as a liposome, as a specimen.

The chromatography techniques in which a capture portion is provided on a carrier such as nitrocellulose, a liquid specimen including analytes and a specimen are permeated on the carrier and the analyte is specifically bound at the capture portion while the other substances are permeated in the downstream direction have been generally used and known in immunochromatography.

However, none of these previous patents provide any teaching for employing the whole blood as a test sample. In Durst et al. (see column 15, lines 20-25), although numerous types of physiologic fluids for example, saliva, sweat, serum, plasma, urine, tear fluid, spinal fluid, etc., are presented a test sample, whole blood is not presented at all. Therefore, contrary to the opinion of the Examiner, we believe that permeation of cell components, such as blood cells, as intended by the present invention, cannot originate from the teachings of Durst et al.

Each of the independent Claims 1 and 23 have been amended to further clarify and distinguish the present invention. To that end, each of these claims has been amended to clarify that the cell components of the claimed biosensor and method move downstream to the detection zone. Support is found in the present disclosure and it is believed that no new matter has been added.

As a result, we believe that Claims 1 and 23 are patentably distinguishable over the cited references of Killen and Durst et al, taken either singly or in combination. For the same reasons we believe that Claims 2-4, 7-11, 24, 25 and 31-34 are allowable since these claims depend from amended Claims 1 and 23, respectively. Reconsideration is respectfully requested.

With regard to the remaining prior art rejections, we believe that Claims 1 and 23 are patentably distinguishable over Killen and Durst et al. for those reasons noted above. The additional citation of Fruitstone et al. (U.S. Patent No. 4,259,207) fails to provide those features that are missing from each of these claims and therefore no obviousness rejection can be maintained. First, Fruitstone et al. teaches technology utilizing the osmotic pressure in a field that uses a reaction solution that is quite different from that in the present invention, which uses a dry sensor. As a result, the field of technology is quite different and we believe this reference would not have been identified by anyone of ordinary skill in the field of the invention.

Assuming, however, in arguendo, that such a combination were possible it is still believed that the combination fails to include all essentially claimed features. Fruitstone et al. relates to a suspension of low ionic strength that enhances immunity hematology agglutination reactions, and this reference teaches that the ion concentration of the solution must be adjusted for the physiological saline, such that when the ion concentration of the solution, i.e., the osmotic pressure is low, the red blood cells will lyse and when the osmotic pressure is high, the red blood cells will become crenated, ant that in order to adjust the ostomic pressure, organic materials such as an amino acid, a sugar, and a soluble alcohol are provided. Nowhere in this reference is there any discussion of those features missing from the combination of Killen and Durst as noted above with regard to either Claim 1 or Claim 23.

Since all of the recited of amended Claims 1 and 23 are not found or suggested, even based on the totality of the teachings of Killeen, Durst et al. and Fruitstone et al, there cannot be a prima facie case of obviousness under the Statute. Reconsideration is therefore respectfully requested with regard to Claims 5, 6 and 26, 27 since these claims merely add further limitations.

Turning to the Section 112 rejections, Applicant has now amended Claims 1 and 23 to clarify the invention. The term "developed" and "chromatographically developed" in Claims 1 and 23 has now been deleted in favor of the term "permeated". Moreover, Applicant has further clarified that the reagent holding part holds a reagent for analyzing an analyte in a liquid specimen and has further clarified

those steps concerning the permeation wherein the shrunk cell components and the liquid specimen are each permeated into the reaction layer in a state in which both the shrunk cell components and the liquid specimen are mixed, the analysis of the analyte being performed in the reaction layer. Claim 23 has also been redrafted such that the steps are now more properly drafted using "–ing" gerunds in addition to the above noted amendments. It is believed that each of the foregoing claim amendments made have been made for purposes of clarity and therefore entry of the amendment is proper under 37 CFR 1.116, as it is believed that no new issues have been created.

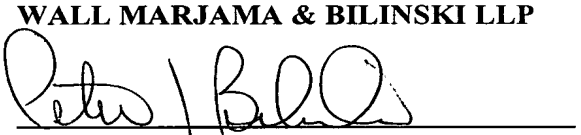
In summary, it is believed the above-captioned patent application is in an allowable condition. Entry of this amendment and an expedited notice of allowability are respectfully requested.

If the Examiner wishes to expedite disposition of the above-captioned patent application, he is invited to contact Applicant's representative at the telephone number below.

The Director is hereby authorized to charge any additional fees associated with this communication or credit any overpayment to Deposit Account No. 50-0289.

Respectfully submitted,

WALL MARJAMA & BILINSKI LLP

By: 

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